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L2 3 FILE ADISINSIGHT
L3 0 FILE ADISNEWS
L4 0 FILE AGRICOLA
L5 0 FILE ANABSTR
L6 0 FILE AQUASCI
L7 0 FILE BIOBUSINESS
L8 0 FILE BIOCOMMERCE
L9 1 FILE BIOSIS
L10 8 FILE BIOTECHDS
L11 2 FILE BIOTECHNO
L12 0 FILE CABA
L13 0 FILE CANCERLIT
L14 4 FILE CAPLUS
L15 0 FILE CEABA-VTB
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L26 0 FILE DRUGNL
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L61          84 FILE USPAT2
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L98        2829 ALBUMIN? (S) (RECOMBINANT# OR MUTA?) AND (SKIN OR HAIR OR CASMET
                IC?) AND (CLEAN? OR CONDITION? OR MOISTURI?)

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CONDITION? OR MOISTURI?)
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L100          0 FILE ADISINSIGHT
L101          0 FILE ADISNEWS
L102          0 FILE AGRICOLA
L103          0 FILE ANABSTR
L104          0 FILE AQUASCI
L105          0 FILE BIOBUSINESS
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L196         25 ALBUMIN? (S) (RECOMBINANT# OR MUTA?) (S) (SKIN OR HAIR OR CASMET
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PROCESSING COMPLETED FOR L196
L197          21 DUP REM L196 (4 DUPLICATES REMOVED)

=> d l197 1-21 ibib abs

L197  ANSWER 1 OF 21  BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-20469  BIOTECHDS
TITLE:            Novel secreted and transmembrane polypeptides and
                  polynucleotides encoding them useful for treating skin,
                  neurodegenerative diseases, as an antithrombotic agent and
                  for inducing endothelial cell apoptosis;
                     recombinant protein production and antagonist and agonist
                     for use in disease gene therapy
AUTHOR:           ASHKENAZI A; BOTSTEIN D; DESNOYERS L; EATON D L; FERRARA N;
                  FILVAROFF E; FONG S; GAO W; GERBER H; GERRITSEN M E; GODDARD
                  A; GODOWSKI P J; GRIMALDI J C; GURNEY A L; HILLAN K J;
                  KLJAVIN I J; MATHER J P; PAN J; PAONI N F; ROY M A; STEWART T
                  A; TUMAS D; WILLIAMS P M; WOOD W I
PATENT ASSIGNEE:  GENENTECH INC
PATENT INFO:      US 2003059772 27 Mar 2003
APPLICATION INFO: US 2001-909064 18 Jul 2001
PRIORITY INFO:    WO 2000-23328 24 Aug 2000; WO 1998-18824 10 Sep 1998
DOCUMENT TYPE:    Patent
```

LANGUAGE: English
OTHER SOURCE: WPI: 2003-540670 [51]
AN 2003-20469 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - An isolated polypeptide (I) having at least 80 % identity to one of 61 130-350 amino acid, secreted and transmembrane polypeptide sequences (S1), given in the specification, or to an amino acid sequence encoded by full length coding sequence of DNA deposited under ATCC Accession No. ATCC 209258, ATCC 209256, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an isolated nucleic acid (II) having at least 80 % nucleic acid sequence identity to a nucleotide sequence that encodes (I); (2) a vector (III) comprising (II); (3) a host cell comprising (III); (4) producing PRO polypeptides; (5) a chimeric molecule (IV) comprising (I) fused to a heterologous amino acid sequence; (6) an isolated antibody (V) that binds specifically to (I); (7) an isolated polypeptide (VI) having at least 80 % amino acid sequence identity to (S1) lacking its associated signal peptide, or an extracellular domain of PRO polypeptide with or lacking its associated signal peptide; and (8) an isolated nucleic acid (VII) having at least 80 % nucleic acid sequence identity to a nucleotide sequence encoding (VI).

WIDER DISCLOSURE - (1) chemically modified derivatives of (I); (2) agonists or antagonists of PRO polypeptides; (3) variants of PRO polypeptides; (4) composition of matter comprising PRO polypeptide, its modulators or antibodies; (5) heteroconjugate antibodies comprising (V); and (6) immunoconjugates comprising (V) conjugated to a cytotoxic agent.

BIOTECHNOLOGY - Preparation: PRO polypeptides are prepared by culturing Chinese Hamster ovary (CHO) cells or Escherichia coli, yeast cells comprising (III) under **conditions** suitable for expression of the polypeptide and recovering the PRO polypeptide from the cell culture. Preferred Vector: (III) operably linked to control sequences recognized by a host cell transformed with the vector. Preferred Molecule: In (IV), the heterologous amino acid sequence is an epitope tag sequence or an Fc region of an immunoglobulin. Preferred Antibody: (V) is a monoclonal, humanized or single-chain antibody.

ACTIVITY - Antipsoriatic; Antiparkinsonian; Nootropic; Neuroprotective; Cytostatic; Dermatological.

MECHANISM OF ACTION - Gene therapy; Inhibitor of tumor cell proliferation; Inhibitor of vascular endothelial growth factor stimulated proliferation of endothelial cells; Enhancer of survival of rod photoreceptor cells; Stimulator of hypertrophy of adult heart; Stimulator of release of proteoglycans from cartilage; Inducer of endothelial cell apoptosis. The ability of PRO polypeptides to induce apoptosis in endothelial cells was tested in human venous umbilical vein endothelial cells. To all wells, 100 micro-l of 0 % serum media complemented with 100 ng/ml vascular endothelial growth factor (VEGF), 0.1 % bovine serum **albumin** (BSA), and 1x penn/strep was added. Test samples containing PRO polypeptides were added in triplicate at dilutions of 1 %, 0.33 % and 0.11 %. Wells without cells were used as a blank and wells with cells only were used as a negative control. As a positive control, 1:3 serial dilutions of 50 micro-l of a 3x stock of staurosporine were used. The cells were incubated for 24-35 hours prior to enzyme linked immunosorbent assay (ELISA). ELISA was used to determine levels of apoptosis. The polypeptide PRO235 tested positive in the test.

USE - PRO1868 polypeptide is useful for detecting PRO245 polypeptide in a sample, or vice versa, by contacting sample comprising cells suspected of expressing the polypeptide to be detected, with the target polypeptide labeled with a detectable label or attached to a solid support, and determining the formation of polypeptide conjugate in the sample. PRO1868 polypeptide is also useful for linking a bioactive molecule to a cell expressing a PRO245 polypeptide, by contacting the cell with PRO1868 polypeptide that is bound to the bioactive molecule and allowing the PRO245 and PRO1868 polypeptides to bind to one another, to link the bioactive molecules to the cell, or vice versa. The bioactive molecule is a toxin, radiolabel or antibody, and causes the death of the

cell. PRO1868 polypeptide or an anti-PRO245 antibody is useful for modulating biological activity of a cell expressing PRO245 polypeptide, or vice versa. Preferably, the cell is killed. (All claimed.) PRO211 and PRO217 polypeptides are useful for treating disorders associated with the preservation and maintenance of gastrointestinal mucosa and the repair of acute and chronic mucosal lesions, **skin** diseases associated with abnormal keratinocyte differentiation (e.g. psoriasis). PRO187 polypeptide is useful for treating Parkinson's disease, Alzheimer's diseases, amyotrophic lateral sclerosis (ALS), neuropathies and additionally, disease related to uncontrolled cell growth, e.g. cancer. PRO219 polypeptide plays a regulatory role in the blood coagulation cascade. PRO246 polypeptides which serves as tumor specific antigens may be exploited as therapeutic targets for anti-tumor drugs. PRO266 polypeptide can be used in assays to determine if it has a role in neurodegenerative diseases or their reversal. PRO269 polypeptide is useful as an antithrombotic agent with reduced risk for hemorrhage as compared with heparin. PRO317 polypeptide is useful in treating PRO317-associated disorders, in modulating endometrial bleeding angiogenesis, and may also have an effect on kidney tissue. (II) is useful in molecular biology including uses as hybridization probes for cDNA library to isolate the full-length PRO cDNA or to isolate other cDNAs, in chromosome and gene mapping, and in the generation of antisense RNA and DNA, and for preparing PRO polypeptides. (II) is also useful for generating transgenic animals or knockout animals which are useful in the development and screening of therapeutically useful reagents. (II) is useful as probes for generating a pool of sequences for identifying related PRO coding sequences, and to construct hybridization probes for mapping the gene which encodes the PRO and for the genetic analysis of individuals with genetic disorders. (II) is useful for recombinantly expressing (I) and for chromosome identification. (I) is useful as molecular marker for protein electrophoresis purposes, and as therapeutic agents. (I) is also useful for screening compounds to identify those that mimic the PRO polypeptide (agonists) or prevent the effect of the PRO polypeptide (antagonists). (I) and (II) are useful for tissue typing. PRO antibodies are useful for immunohistochemical staining and/or assay of sample fluids. Anti-PRO antibodies are useful in diagnostic assays for PRO e.g. detecting its expression in specific cells, tissues or serum, and for affinity purification of PRO from **recombinant** cell culture or natural sources.

ADMINISTRATION - Administered by intravenous, intraperitoneal, intracerebral, intramuscular, intraocular, intraarterial, intralesional or topical route. PRO polypeptide is administered at a dose of 10 ng-100 mg/kg, preferably 1 micro-g/kg-10 mg/kg/day.

EXAMPLE - The extracellular domain (ECD) sequences from 950 known secreted proteins from the Swiss-Prot public database were used to search expressed sequence tag (EST) databases. The EST databases included public databases and proprietary databases. The search was performed using the computer program BLAST or BLAST-2. Those comparisons with a BLAST score of 70 or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program phrap. Using this extracellular domain homology screen, consensus DNA sequences were assembled relative to the other identified EST sequences using phrap. Based upon the consensus sequences obtained, oligonucleotides were then synthesized and used to identify by PCR a cDNA library that contained the sequence of interest and for use as probes to isolate a clone of the full-length coding sequence for a PRO polypeptide. A consensus DNA sequence was assembled relative to the other identified EST sequences, where the consensus sequence was designated as DNA30857. An EST proprietary to Genentech was employed in the consensus assembly. The EST was designated as DNA20088. Based on the DNA30857 consensus sequence, oligonucleotides were synthesized to identify by PCR a cDNA library that contained the sequence of interest and for use as probes to isolate a clone of the full-length coding sequence for PRO230. A pair of PCR primers (forward and reverse) were synthesized: forward PCR primer 5'-TTCGAGGCCTCTGAGAAGTGGCCC-3', and reverse PCR primer5'-

GGCGGTATCTCTCTGGCCTCCC-3'. Additionally, a synthetic oligonucleotide hybridization probe was constructed from consensus DNA30857 sequence which had the sequence 5'-TTCTCCACCGCAGCTGTGGCATCCGATCGTGTCTCAATCCATTCTCT GGG-3'. In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO230 gene using the probe oligonucleotide and one of the PCR primers. DNA sequencing of the clones isolated gave the full-length DNA sequence for PRO230. The predicted polypeptide precursor was 467 amino acids long.(470 pages)

L197 ANSWER 2 OF 21 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
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TITLE: New secreted and transmembrane PRO polypeptides, useful for treating cancer, skin disorders, neurodegenerative diseases, and for lessening the effects of viral infection; recombinant protein production and antagonist and agonist for use in disease gene therapy
AUTHOR: ASHKENAZI A; BOTSTEIN D; DESNOYERS L; EATON D L; FERRARA N; FILVAROFF E; FONG S; GAO W; GERBER H; GERRITSEN M E; GODDARD A; GODOWSKI P J; GRIMALDI J C; GURNEY A J; HILLAN K J; KLJAVIN I J; MATHER J P; PAN J; PAONI N F; ROY M A; STEWART T A; TUMAS D; WILLIAMS P M; WOOD W I
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AN 2003-20054 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - An isolated polypeptide (I) having at least 80% amino acid sequence identity to 49 secreted and transmembrane polypeptides having a sequence (S1) chosen from 61 fully defined sequences given in specification, such as a sequence of 353, 379, 164, 189, 205, 660, 915, 390, 690, or 216 amino acids, or to an amino acid sequence encoded by the full length coding sequence of DNA with ATCC Accession Nos. given in the specification, is new.

DETAILED DESCRIPTION - An isolated polypeptide (I) having at least 80% amino acid sequence identity to 49 secreted and transmembrane polypeptides named as PRO211, PRO217, PRO230, PRO232, PRO187, PRO265, PRO219, PRO228, PRO533, PRO245, and PRO246 having a sequence (S1) chosen from 61 fully defined sequences given in specification, such as a sequence of 353, 379, 164, 189, 205, 660, 915, 390, 690, or 216 amino acids, or to an amino acid sequence encoded by full length coding sequence of DNA deposited under ATCC Accession Nos. given in the specification, such as ATCC 209258, 209256, 209264, 209250, 209375, 209378, 209384, 209396, 209420, 209480, 209265, 209257, 209262, 209253, 209402, 209401, and 209397. INDEPENDENT CLAIMS are also included for: (1) an isolated nucleic acid (II) having at least 80% nucleic acid sequence identity to a nucleotide sequence that encodes (I); (2) a vector (III) comprising (II); (3) a host cell comprising (III); (4) producing PRO polypeptides; (5) a chimeric molecule (IV) comprising (I) fused to a heterologous amino acid sequence; (6) an isolated antibody (V) that binds specifically to (I); (7) an isolated polypeptide (VI) having at least 80% amino acid sequence identity to (S1) lacking its associated signal peptide, or an extracellular domain of PRO polypeptide with or lacking its associated signal peptide; and (8) an isolated nucleic acid (VII) having at least 80% nucleic acid sequence identity to a nucleotide sequence encoding (VI).

WIDER DISCLOSURE - Also disclosed as new are: (1) chemically modified derivatives of (I); (2) agonists or antagonists of PRO polypeptides; (3) variants of PRO polypeptides; (4) a composition comprising PRO polypeptide, its modulators or antibodies; (5)